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Dyspnoea and hypoxaemia after lung surgery: the role of interatrial right-to-left shunt

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ABSTRACT: **After lung surgery, some patients complain of unexplained increased dyspnoea associated with hypoxaemia. This clinical presentation may be due to an interatrial right-to-left shunt despite normal right heart pressure. Some of these patients show postural dependency of hypoxaemia, whereas others do not.**

In this article, the pathogenesis and mechanisms involved in this post-surgical complication are discussed, and the techniques used for confirmation and localisation of shunt are reported.

An invasive technique, such as right heart catheterisation with angiography, was often used in the past as the diagnostic procedure for the visualisation of interatrial shunt. As to noninvasive techniques, a perfusion lung scan may be used as the first approach as it may detect the effect of the right-to-left shunt by visualising an extrapulmonary distribution of the radioactive tracer. The 100% oxygen breathing test could also be used to quantify the amount of right-to-left shunt. Particular emphasis is given to newer imaging modalities, such as transoesophageal echocardiography, which is minimally invasive but highly sensitive in clearly visualising the atrial septum anatomy.

Finally, the approch to closure of the foramen ovale or atrial septal defect is discussed. Open thoracotomy was the traditional approach in the past. Percutaneous closure has now become the most used and effective technique for the repair of the interatrial anatomical malformation.

KEYWORDS: **Heart septal defect, lung surgery, postural hypoxaemia**

Patients who have undergone pulmonary resection commonly complain of dyspnoea, which is frequently attributed to the loss of alveolar volume and restriction of the pulmonary vascular bed [1, 2].

However, some of these patients show a sudden and unexplained onset of dyspnoea due to an interatrial right-to-left shunt through a previously asymptomatic patent foramen ovale (PFO) or atrial septal defect (ASD) with normal right heart pressure [3–6].

One of the peculiar aspects of this complication is its possible association with so-called platypnoea (flat breathing), defined as dyspnoea induced by upright posture and relieved by recumbency [7], and orthodeoxia, defined as arterial oxygen desaturation accentuated by upright posture and improved by recumbency [8].

Two previous reviews of the literature [5, 6] reported several cases of patients observed during the period 1956–1992 who showed a right-to-left interatrial shunt after lung surgery that, in most instances, was associated with platypnoea–orthodeoxia syndrome. This syndrome occurred a month to several months after pulmonary resection and was not associated with pulmonary hypertension [3–5, 9–29].

By contrast, there have been only a few reports describing dyspnoea and hypoxaemia due to an interatrial right-to-left shunt occurring shortly after lung surgery [23, 30–38]. In most instances, these respiratory manifestations were not posture-dependent.

The peculiarity of this post-surgical complication prompted the present review of the data reported in the literature to gain insight into its pathogenesis.

METHODS

The PubMed database was searched for all case reports dealing with the occurrence of dyspnoea and hypoxaemia after lung surgery due to an interatrial right-to-left shunt. Bibliographies from

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pertinent articles and two previous reviews [5, 6] were also scanned for suitable articles on this topic.

The search identified 33 studies concerning 46 patients during the period 1956–2004, all included in the final analysis.

Data on age, sex and the methods used for the diagnosis were evaluated. Separate lists were made of those cases who showed a sudden onset of respiratory symptoms $\geqslant$1 month following lung surgery (group A) and those in whom the symptoms occurred within 1 month after the surgical procedure (group B). The following factors were taken into account: 1) the number of patients in each study; 2) the type of surgery performed; 3) the interval between surgery and the onset of symptoms (symptomless interval); 4) the cause of the shunt; and 5) arterial oxygen tension (P_{a,O_2}) or saturation (S_{a,O_2}) in the sitting and supine positions, in order to assess the posture dependency of dyspnoea and hypoxaemia, platypnoea–orthodeoxia syndrome, based on the changes in arterial blood gas data, whenever reported in the sitting and supine position, or, if lacking, the description of the clinical findings in each report, already assigned as posture dependency in the two previous reviews [5, 6]. In the former event, the presence of platypnoea–orthodeoxia syndrome was assessed according to its current definition, *i.e.* a $\geqslant$10% increase in baseline S_{a,O_2} or P_{a,O_2} on moving from the sitting to the supine position [39]. In addition, the right atrial pressure, left atrial pressure and pulmonary arterial pressure, as well as the treatment used to close the shunt, and the follow-up of patients were also reported.

Statistics

Whenever appropriate, the two-tailed paired or unpaired t-test, Levene's test for equality of variance and Fisher's exact test were used to compare haemodynamic parameters, such as mean right atrial pressure, mean left atrial pressure and mean pulmonary arterial pressure, within each group, as well as their differences between groups. Data are reported as mean$\pm$SD. A p-value of <0.05 was considered significant throughout.

RESULTS

The mean age of the patients listed in tables 1 and 2 (group A; 34 males and two females) was 59$\pm$9 yrs and of those in tables 3 and 4 (group B; eight males and two females) it was 65$\pm$9 yrs (p=0.10).

Type of lung surgery

The surgical procedures involved in group A (table 1) were: right pneumonectomy in 24 patients (67%), left pneumonectomy in eight (22%) and right lobectomy in three (8%). In one patient, who underwent thoracotomy due to lung cancer, the type of operation was not reported. The types of surgical procedure in group B (table 2) were: right pneumonectomy in six patients (60%), right lobectomy in three (30%) and left pneumonectomy in one (10%).

Overall, the right side of the chest was more frequently (36 out of 45 (80%)) involved than the left (nine out of 45 (20%)), and lung cancer was the disease affecting all patients.

Symptomless period

Table 1 shows the cases in which dyspnoea occurred $\geqslant$1 month following lung surgery; their symptomless period ranged 1–31 months (mean 6$\pm$7 months).

Table 3 shows the cases in which dyspnoea occurred within 1 month after lung surgery; their symptomless period ranged 1–7 days (mean 3$\pm$3 days).

Prevalence of congenital abnormality

Regarding the prevalence of congenital abnormality of the right atrium causing right-to-left shunt, PFO was more frequent by far than ASD: 78% (28 out of 36) of patients in group A, and 100% in group B. Regarding the ASD abnormalities, all listed in table 1 (eight out of 36 (22%) patients), the interatrial communication was of the secundum type in five patients, whereas the type was not specified in two patients. In one patient, an atrial septal aneurysm was found at the level of the fossa ovalis.

Type of investigation for the diagnosis

Regarding diagnostic work-up in these patients, 16 out of the 36 (44%) patients in group A underwent the 100% oxygen breathing test. In a few of them, the test was performed in both the recumbent and the upright position. In group B, four out of the 10 (40%) patients underwent the 100% oxygen breathing test.

A perfusion lung scan, which is usually performed to rule out pulmonary embolism in such patients, was obtained in 17 out of 36 (47%) patients in group A and five out of 10 (50%) patients in group B. Nine out of the 17 (56%) perfusion lung scans performed in patients from group A showed no perfusion abnormality, whereas, in the seven other patients, the lung scan showed an extrapulmonary distribution of the radioactive tracer in the brain, thyroid, kidneys and spleen, suggesting the presence of right-to-left shunt [40]. Interestingly, in one of these seven patients, the pattern of extrapulmonary distribution of radioactive tracer was neglected, and, in another patient, the extrapulmonary uptake of the radiotracer became evident 1 month after the initial evaluation, when deterioration of respiratory symptoms had occurred. Of the five lung scans performed in the 10 patients from group B, three did not show any perfusion abnormality, and two showed extrapulmonary uptake of the radioactive tracer.

Tests for the diagnosis of right-to-left intracardiac shunt

Among the 36 patients in group A, intracardiac shunt through PFO or ASD was demonstrated by inferior and/or superior vena cava angiography in 17 (47%) patients, contrast transthoracic or transoesophageal echocardiography in 15 (41%) and right heart catheterisation in two (6%), and, in one (3%) patient each, by magnetic resonance imaging and open heart surgery.

Regarding the 10 patients in group B, the final diagnosis of intracardiac right-to-left shunt was made by contrast transthoracic or transoesophageal echocardiography in eight (80%) patients and right heart catheterisation in two (20%).

Overall, the techniques more frequently used for the diagnosis of intracardiac right-to-left shunting in this series of 46 patients were, in order, angiography (17 patients), contrast

TABLE 1 Clinical characteristics of patients with sudden-onset respiratory symptoms occurring ⩾1 month following lung surgery (group A)

First author [ref.]	Case No.	Surgery	Symptomless interval months	Shunt cause	Posture-dependent
SCHNABEL [3]	1	RP	1	PFO	+
WINTERS [4]	2	RP	3	ASD	+
BEGIN [9]	3	RP	2	ASD	+
WRANNE [10]	4	LP	1	PFO	+
HOLTZMAN [11]	5	RP	1.5	ASD	-
LABRESH [12]	6	LP	5	ASD	+
ROOS [13]	7	LP	2	PFO	+
SPRINGER [14]	8	RL	4	PFO	+
SEWARD [15]	9	RP	7	PFO	+
	10	LP	5	PFO	+
	11	RP	1#	PFO	+
	12	LP	11	PFO	+
FRANCO [16]	13	RP	4	PFO	+
WIHLM [5]	14	RP	2	PFO	+
VAN ROSSUM [17]	15	RP	3	PFO	+
	16	RP	2	PFO	+
	17	RP	4	PFO	+
	18	RP	27	PFO	+
SMEENK [18]	19	LP	2	PFO	+
DARREMONT [19]	20	RP	3	PFO	+
BUSS [20]	21	RP	6	PFO	+
TIMMERMANS [21]	22	RP	1	ASA	+
	23	RP	1	ASD	+
MERCHO [22]	24	RP	6	PFO	+
	25	RP	12	PFO	+
LANDZBERG [23]	26	RL	31	PFO	+
	27	THOR	15	PFO	+
	28	RL	3	PFO	+
ARNAUD-CROZAT [24]	29	LP	6	ASD	-
DURAND [25]	30	LP	5	ASD	-
BAKRIS [26]	31	RP	3	PFO	+
	32	RP	3	PFO	+
VINCENT [27]	33	RP	6	PFO	+
DANNER [28]	34	RP	3	PFO	+
	35	RP	3	PFO	+
MARINI [29]	36	RP	5	PFO	+

RP: right pneumonectomy; LP: left pneumonectomy; RL: right lobectomy; THOR: thoracotomy; PFO: patent foramen ovale; ASD: atrial septal defect; ASA: atrial septal aneurysm; +: posture-dependent dyspnoea; -: posture-independent dyspnoea. #: 10 yrs after diagnosis of right-to-left shunt.

transoesophageal echocardiography (12) and contrast transthoracic echocardiography (11).

Posture-dependent abnormalities in gas exchange

As shown in table 1, platypnoea–orthodeoxia syndrome was present in 33 out of the 36 (92%) patients in group A, and it occurred ⩾1 month after lung surgery. In 19 of these subjects, the finding of platypnoea–orthodeoxia was supported by sitting–supine changes in P_{a,O_2} or S_{a,O_2} (table 2) according to the definition reported above [39]. Of the 10 patients who complained of acute dyspnoea shortly after lung surgery, three manifested platypnoea–orthodeoxia syndrome and sitting–supine changes in P_{a,O_2} or S_{a,O_2} (table 3 and 4).

Haemodynamic measurement

The information regarding haemodynamic parameters is fragmentary. From the available data shown in table 2 (group A), it appears that mean right atrial pressure was 4.3±3.4 mmHg in 27 out of the 36 (75%) patients, mean left atrial pressure was 6.0±3.5 mmHg in 22 (61%) and mean pulmonary arterial pressure was 14.3±3.7 mmHg in 26 (72%; table 5). Thus, in the patients in group A, the mean pressure gradient between the left and right atrium was 1.07±3.3 mmHg, and the mean pulmonary arterial pressure was normal (table 5).

In group B (table 5), mean right atrial pressure was 7.6±3.7 mmHg in eight out of 10 (80%) patients, whereas mean left

TABLE 2 Arterial blood gas levels, haemodynamic data and outcome of patients with sudden-onset respiratory symptoms occurring ≥1 month after lung surgery (group A)

First author [ref.]	P_{a,O_2} mmHg		S_{a,O_2} %		$\bar{P}ra$ mmHg	$\bar{P}la$ mmHg	$\bar{P}pa$ mmHg	Shunt closure method	Follow-up
	Sitting	Supine	Sitting	Supine					
SCHNABEL [3]	NR	NR	NR	NR	NR	NR	NR	Open-chest surgery	A; 2 yrs
WINTERS [4]	48	78	NR	NR	NR	NR	NR	Open-chest surgery	A; 1 yr
WIHLM [5]	42	NR	NR	NR	NR	NR	NR	No closure	D (ARF); 1 month
BEGIN [9]	34	55	NR	NR	15	12	NR	Open-chest surgery	NR
WRANNE [10]	50	64	NR	NR	-1	NR	12	No closure	A; 21 months
HOLTZMAN [11]	NR	34	NR	NR	3	6	15	Open-chest surgery	D (septic shock); 2 days
LABRESH [12]	36	NR	NR	NR	0	NR	8	Open-chest surgery	A; 1 yr
ROOS [13]	40	47	NR	NR	0	NR	9	Open-chest surgery	A; 8 months
SPRINGER [14]	44#	81#	NR	NR	4	10	13	Open-chest surgery	NR
SEWARD [15]	71	NR	NR	NR	6	9	16	Open-chest surgery	A; 8 yrs
	43	56	NR	NR	1	8	16	Open-chest surgery	D (massive CI); 7 days
	62	72	NR	NR	2	7	20	No closure	A; 8 months
	65	NR	NR	NR	6	14	13	Open-chest surgery	NR
FRANCO [16]	NR	NR	NR	NR	5	5	14	Open-chest surgery	A; 1 yr
VAN ROSSUM [17]	NR	NR	NR	NR	4	5	13	Open-chest surgery	A; 2–10 months¶
	NR	NR	NR	NR	2	2	14	Open-chest surgery	A; 2–10 months¶
	NR	NR	NR	NR	3	2	8	Open-chest surgery	A; 2–10 months¶
	NR	NR	NR	NR	3	NR	11	Open-chest surgery	A; 2–10 months¶
SMEENK [18]			68.5	NR	4	2	10	Open-chest surgery	A; discharge
DARREMONT [19]			83	92	10	7	17	Open-chest surgery	A; 1 yr
BUSS [20]			75	87	5	NR	13	Open-chest surgery	A; 5 yrs
TIMMERMANS [21]	33+	57+	NR	NR	4.5	2.5	15	Open-chest surgery	A; discharge
	NR	NR	NR	NR	4.5	3.5	14	Open-chest surgery	A; discharge
MERCHO [22]	NR	NR	83§	92§	NR	NR	NR	Open-chest surgery	A; discharge
	NR	NR	47§	56§	NR	NR	NR	Open-chest surgery	A; discharge
LANDZBERG [23]	NR	NR	70/80	98	7	7	19	Transcatheter	A; 50 months
	NR	NR	70/80	94	3	7	16	Transcatheter	A; 44 months
	NR	NR	70/80	93	4	4	22	Transcatheter	D (tumour progression); 2 months
ARNAUD-CROZAT [24]	NR	NR	NR	60/90	2	0	17	Open-chest surgery	A; 2 yrs
DURAND [25]	49	NR	NR	NR	NR	NR	NR	No closure	NR
BAKRIS [26]	NR	NR	81	99	5	7	16	Open-chest surgery	A; discharge
	NR	NR	75	NR	11	9	20	Open-chest surgery	A; discharge
VINCENT [27]	51	61	NR	NR	NR	NR	NR	Transcatheter	A; 1.5 months
DANNER [28]	NR	NR	80	93	NR	NR	NR	Open-chest surgery	A; 7 months
	NR	NR	83	92	NR	NR	NR	Open-chest surgery	A; discharge
MARINI [29]	43	74	NR	NR	3	3	11	Transcatheter	A; 2 yrs

P_{a,O_2}: arterial oxygen tension; S_{a,O_2}: arterial oxygen saturation; $\bar{P}ra$: mean right atrial pressure; $\bar{P}la$: mean left atrial pressure; $\bar{P}pa$: mean pulmonary arterial pressure; NR: not reported; A: alive; D: dead; CI: cerebral infarction; ARF: acute respiratory failure. #: breathing 40% oxygen; ¶: follow-up of these patients ranged 2–10 months; +: breathing 3.5 L·min^{-1} oxygen; §: breathing 100% oxygen. 1 mmHg=0.133 kPa.

atrial pressure was 7.1±3.6 mmHg in seven (70%) patients and mean pulmonary arterial pressure 21.8±10.7 mmHg in six (60%). Interestingly, the mean right atrial pressure in patients in group B was significantly higher than that of patients in group A (7.6±3.7 *versus* 4.3±3.4 mmHg, respectively; $p<0.05$; table 5). The mean pulmonary arterial pressure in patients in group B (21.8±10.7 mmHg) was also higher than that of patients in group A (14.3±3.7 mmHg), although the difference did not attain significance ($p=0.15$).

Closure of interatrial communication

Overall, the methods used to close a PFO or ASD in these 46 patients were: open-chest surgical closure in 32 (70%) patients, transcatheter permanent implantation of a device placed across the interatrial communication [23] in eight (17%) and a pulmonary arterial catheter with a balloon inflated in the left atrium for temporary closure in one (2%; table 2). In the five (11%) other patients, four in group A (table 2) and one in group B (table 4), the interatrial communication was not closed. Indeed,

TABLE 3 Clinical characteristics of patients with sudden-onset respiratory symptoms occurring within 1 month of lung surgery (group B)

First author [ref.]	Case No.	Surgery	Symptomless interval days	Shunt cause	Posture-dependent
DLABAL [30]	1	RP	7	PFO	-
VACEK [31]	2	RL	3	PFO	-
HAZARD [32]	3	RP	2	PFO	-
BERRY [33]	4	LP	1	PFO	+
SAADA [34]	5	RP	1	PFO	-
LANDZBERG [23]	6	RL	7	PFO	+
GODART [35]	7	RP	2	PFO	-
ALFAIFI [36]	8	RL	7	PFO	-
GODART [37]	9	RP	2	PFO	NR
MALL [38]	10	RP	2	PFO	+

RP: right pneumonectomy; RL: right lobectomy; LP: left pneumonectomy; PFO: patent foramen ovale; NR: not reported; +: posture-dependent dyspnoea; -: posture-independent dyspnoea.

TABLE 4 Arterial blood gas levels, haemodynamic data and outcome of patients with sudden-onset respiratory symptoms occurring within 1 month of lung surgery (group B)

First author [ref.]	P_{a,O_2} mmHg		S_{a,O_2} %		$\bar{P}_{ra}$ mmHg	$\bar{P}_{la}$ mmHg	$\bar{P}_{pa}$ mmHg	Shunt closure method	Follow-up
	Sitting	Supine	Sitting	Supine					
DLABAL [30]	156#	148#	NR	NR	10	6	20	Open-chest surgery	A; 21 months
VACEK [31]	NR	50	NR	NR	4	2	10	Open-chest surgery	A; discharge
HAZARD [32]	NR¶	64¶	NR	NR	14	12	41	Balloon inflated in left atrium	D (pneumothorax); 2 days
BERRY [33]	NR	NR	55	71	5	NR	20	Open-chest surgery	D (sepsis); 1 month
SAADA [34]	NR	46	NR	NR	7	10	25	No closure+	D (cancer progression); 2 months
LANDZBERG [23]	NR	NR	80/90	95	6	6	15	Transcatheter	D (cancer progression); 3 months
GODART [35]	NR	NR	NR	NR	4	4	NR	Transcatheter	A; 6 months
ALFAIFI [36]	40	NR	NR	NR	NR	NR	NR	Open-chest surgery	A; discharge
GODART [37]	NR	NR	NR	NR	11	10	NR	Transcatheter	D (septic shock); 1 day
MALL [38]	50	72	NR	NR	NR	NR	NR	Open-chest surgery	A; discharge

P_{a,O_2}: arterial oxygen tension; S_{a,O_2}: arterial oxygen saturation; $\bar{P}_{ra}$: mean right atrial pressure; $\bar{P}_{la}$: mean left atrial pressure; $\bar{P}_{pa}$: mean pulmonary arterial pressure; NR: not reported; A: alive; D: dead. #: breathing 100% oxygen; ¶: breathing 40% oxygen; +: hypoxaemia spontaneously relieved and surgical closure not considered free of risk. 1 mmHg=0.133 kPa.

patient No. 4 showed marked clinical improvement once diuretics and digoxin were withdrawn [10], patient No. 11 was followed up for 8 months after diagnosis and the surgical intervention was still under consideration at the time of the report [15], patient No. 14 was deemed too ill to undergo surgery [5] and patient No. 30 did not undergo surgery owing to a very poor prognosis due to the progression of lung cancer [25]. Patient No. 5 in group B did not undergo surgical intervention, in part due to the spontaneous partial improvement of clinical symptoms, but mainly due to a poor prognosis [34].

Follow-up studies

In table 2, the follow-up of patients of group A is reported. Overall, four out of the 36 (11%) patients died, two of them a few days after surgery.

Sixteen (50%) patients were followed-up for a mean period of 26±25 months (range 1.5–96 months). In eight (25%) patients, the follow-up ended at the time of their discharge from the hospital, in four (12.5%) it ranged 2–10 months, and, in the remaining four (12.5%), the follow-up period was not reported (table 2).

TABLE 5 Comparison of haemodynamic variables in the two groups of patients

	Group A	Group B	p-value
Subjects n	36	10	
$\bar{P}$ra			
mmHg	4.3±3.4	7.6±3.7	0.02
n (%)	27 (75)	8 (80)	
$\bar{P}$la			
mmHg	6.0±3.5	7.1±3.6	0.42
n (%)	22 (61)	7 (70)	
$\bar{P}$pa			
mmHg	14.3±3.7	21.8±10.7	0.15
n (%)	26 (72)	6 (60)	
$\bar{P}$la–$\bar{P}$ra			
mmHg	1.07±3.3	-0.86±2.2	0.16
n (%)	23 (64)	7 (70)	

Data are presented as mean±SD, unless otherwise stated. $\bar{P}$ra: mean right atrial pressure; $\bar{P}$la: mean left atrial pressure; $\bar{P}$pa: mean pulmonary arterial pressure. 1 mmHg=0.133 kPa.

Regarding patients in group B (table 4), death occurred in five out of 10 (50%) patients, with two dying 1 day and 3 months after transcatheter PFO closure, respectively. Of the five patients who survived, three were followed-up until hospital discharge, one was followed-up for 6 months, one for 21 months, after PFO closure (table 4).

DISCUSSION

From the survey of the literature, 46 cases of patients who had undergone pulmonary resection and developed, over a variable period of time after surgery, unexplained dyspnoea with hypoxaemia that, in several cases, was posture-dependent were reviewed. This surgical complication was due to an interatrial right-to-left shunt through a PFO or ASD with normal right heart pressures.

Mechanisms involved in right-to-left shunt

The type and site of pulmonary resection do not appear to affect the time of onset of right-to-left shunt. Indeed, it occurred after right pneumonectomy, as well as after resection of a few pulmonary segments.

Similarly, the nature of the congenital abnormality, be it PFO or ASD, does not in itself explain the time of occurrence of right-to-left shunting. Indeed, both of these congenital abnormalities were usually asymptomatic before pulmonary resection [18].

By grouping patients as a function of the symptomless interval, it was found that platypnoea–orthodeoxia syndrome was present in 92% of patients of group A (table 1), in whom the symptomless interval averaged 6±7 months. On the contrary, in the 10 patients of group B (table 3), in whom the symptomless interval was 3±3 days, platypnoea–orthodeoxia syndrome was present in three out of the nine (33%) patients for whom these data were available (table 3). Thus, the syndrome was significantly more frequent in patients in whom respiratory symptoms developed several months after lung surgery ($p<0.001$; Fisher's exact test).

The late occurrence of symptoms in patients with platypnoea–orthodeoxia (group A; table 1) may be the result of relatively slow anatomical remodelling after lung resection. Indeed, the obliteration of the post-pneumonectomy space usually takes 3 weeks to 7 months [41]. The shift of the mediastinum towards the operated side may be extensive when the obliteration of the pleural space is complete. In this case, the interatrial stretching can be conspicuous [42] and right-to-left shunting through a PFO or an ASD may develop (mainly in the upright position) despite normal right atrial pressure [8]. The interatrial stretching seems to be the mechanism of the streaming of blood from the inferior vena cava to the left atrium in the absence of a pressure gradient, particularly in the presence of mediastinal distortion, when the right atrium is shifted away, while the inferior vena cava remains fixed in position [16]. This mechanism appears operative in patients of group A, despite the fact that the mean left atrial pressure was higher than the mean right atrial pressure (table 5). However, it has been suggested recently that the mobility of the fossa ovalis membrane might favour and enhance the flow towards the foramen ovale [43]. This additional mechanism seems to be operative during mid-systole, when a pronounced motion of the atrial septum toward the left atrium occurs [44]. Furthermore, as shown in table 5, the mean pulmonary arterial pressure was normal (14.3±3.7 mmHg). Therefore, the occurrence of right-to-left shunting through a pressure gradient mechanism appears unlikely in these patients.

In group B, the mean right atrial pressure was higher than the mean left atrial pressure in four of the seven patients in whom these data were available (table 4). By comparing the mean right atrial pressure between the two groups (table 5), it appears that the mean right atrial pressure in most patients of group B was significantly higher than that found in patients of group A (7.6±3.7 *versus* 4.3±3.4 mmHg; $p<0.05$). Moreover, the mean pulmonary arterial pressure was higher in patients of group B than in those of group A.

Thus, in this case, the shunt could occur as a consequence of a sudden increase in pulmonary vascular resistance and a decrease in right ventricular compliance [45] following surgical reduction of the pulmonary vascular bed [18]. In addition, the intra- and perioperative fluid overload, which is known to impair right heart function in pulmonary resection [46, 47], could also act through the same mechanism in these patients.

Interestingly, three of the 10 patients in group B showed platypnoea–orthodeoxia syndrome, although it has been demonstrated that this complication more frequently occurs as a late post-pneumonectomy complication.

In case No. 4 (group B), who underwent left pneumonectomy, the mean right atrial and pulmonary arterial pressures were higher than the corresponding mean pressures of patients in group B (tables 4 and 5). Therefore, the sudden increase in flow in the right lung may have caused an interatrial right-to-left shunt in this patient, with a further increase in the fraction of shunted blood in the sitting position. In case No. 6 (group B), the mean pressure in both atria was identical and the right-to-left shunt could occur on moving to the sitting position due to a gravity-dependent increase in blood flow [48]. Thus, the pressure gradient mechanism seems to be the trigger of this clinical feature, even in two of the three cases who showed posture dependency of shunt shortly after surgery. Conversely, six out of the seven (86%) patients with available data in group B exhibited a baseline mean right atrial pressure higher than, or at least equal to, that of the left atrium.

Diagnostic and therapeutic management

Once the suspicion of right-to-left shunt is raised, the 100% oxygen breathing test may be useful, particularly when it is performed in the sitting and supine position. Indeed, it appears that 20 out of the 46 (43%) patients reported here had P_{a,O_2} while breathing 100% oxygen that were compatible with the presence of right-to-left shunting.

A perfusion lung scan may also show findings suggestive of right-to-left shunt, such as extrapulmonary distribution of radioactive tracer in the brain, thyroid, kidneys and spleen, particularly when the radiotracer injection is performed with the patient in the sitting position [25, 29].

In order to confirm the diagnosis of interatrial right-to-left shunt, right heart angiography was the technique more frequently used until 1988 [28]. Nowadays, it has been progressively replaced by contrast transthoracic or transoesophageal echocardiography, performed in 29 (63%) patients in the present series. Indeed, the latter technique is far less expensive and less invasive than angiography, although equally reliable.

Regarding the procedure used to close the interatrial shunt, open-chest surgery was the technique of choice in 32 out of the 46 (70%) patients of the present series. Since the mid-1990s, open heart surgery has been progressively replaced by transcatheter device implantation across the interatrial communication. This therapeutic option has been successfully applied in 78 patients from the French PFO registry who had platypnoea–orthodeoxia syndrome of various aetiology [49].

Follow-up of patients

Follow-up data show that nine patients died, four (11%) from group A and five (50%) from group B. Of these patients, only four died within a few days after interatrial communication closure, three of them after surgery and one after transcatheter device implantation.

The high rate of death of patients in group B is probably accounted for by their poor clinical conditions, as suggested, on the basis of the available data, by their very low P_{a,O_2} and/or S_{a,O_2}. The occurrence of death in this group of patients appears independent of the method used to close the interatrial communication, be it surgery or transcatheter device implantation.

CONCLUSIONS

The mechanism of occurrence of posture-dependent hypoxaemia seems to characterise a population of patients in whom right-to-left shunt is a late complication of post-surgical intrathoracic anatomical remodelling.

Conversely, in those patients in whom hypoxaemia occurs shortly after thoracic surgery, right-to-left shunt seems to be induced by a decrease in right ventricular compliance following a reduction of the pulmonary vascular bed and/or by the intra- and perioperative fluid overload, which, in turn, may generate a right-to-left atrial pressure gradient.

Regarding the diagnosis of this post-surgery complication, contrast echocardiography (either transthoracic or transoesophageal) appears a safe and reliable technique.

Finally, regarding treatment, the use of transcatheter device implantation seems to be an effective and minimally invasive approach to this syndrome.

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